It had previously been shown that it was not present in the posterior urethra. The bladder urine was studied by aspirating it under aseptic conditions in routine cases at postmortem in the Johns Hopkins Hospital. In the first case thus studied I was surprised to find in the urine, after centrifugation and staining, many large clumps of organisms deeply stained with the carbol-fuchsin. These were at first interpreted as smegma bacilli, but on looking up the pathological report of the case it was found to be one of advanced general miliary tuberculosis, with lesions in the kidney, ureters, and bladder. This patient had gone to autopsy with a doubtful diagnosis. I then looked over the histories of the cases of general miliary tuberculosis at the Johns Hopkins Hospital and found that in nearly every instance in which the urine was examined for the organisms they were found present; but that in the majority of instances no urinary examination for tubercle bacilli had been made, although the sputum had been examined with great care. The point brought out by these observations is that in suspected general miliary tuberculosis (a disease, as is well-known, readily confused with typhoid fever and other febrile conditions) the urine should be examined for tubercle bacilli, for the value of urinary examination in these cases is far greater than that of sputum examination.

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# ALBUMIN IN THE SPUTUM IN TUBERCULOSIS: ITS VALUE IN DIAGNOSIS AND PROGNOSIS.[1]

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Doubtless we shall always place our chief dependence upon physical examination for the recognition of pulmonary tuberculosis; however, there are times when even the keenest examiner would like to have corroboration of the suspicions which have been aroused by his findings on physical examination. Of the numerous tests applied to such suspects, in the hope or expectation of confirmation of the diagnosis of tuberculosis, such as the various tuberculin reactions (the cutaneous of von Pirquet, the subcutaneous, the percutaneous of Moro, and others; the intradermal of Mantoux and the ophthalmic of Calmette); the sero-agglutination of Arloing and Courmont; the precipitin test of Bonomé and Vincent and Combes; Wright's opsonic index; anaphylaxis (Marmorek); the cobra poison reaction; and finally the fixation test, all leave something wanting. Some, or rather most, of these require too elaborate laboratory facilities and too skilled workers to be at the command of the general practitioner, and others are of such dilicacy as to give positive results in febrile conditions other than tuberculosis; and all of them are open to the criticism that they fail to show whether the patient who reacts is suffering from active, latent, or healed tuberculosis. In an effort to find some simple means by which any physician can corroborate clinical suspicions or evidences of pulmonary tuberculosis the albumin reaction in the sputum has of late come into vogue, with the hope of furnishing conclusive evidence of active tuberculosis or by a negative finding excluding the possibility of tuberculosis. It was with the hope of determining for our own future guidance and dependence the exact value of this addition to our diagnostic and prognostic methods that we have undertaken the examination of the sputum in a certain number of cases with a survey of the available literature, the results of which we now present.

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[1] Read before the North Carolina State Medical Association at the annual meeting at Raleigh, June 16, 1914.

The first mention of albumin in the sputum was made by Biemer,[2] in 1855. The statement attracted no particular attention, though Wanner, in 1903, stated that all sputa contained albumin, liberated through decomposition. However, the attention of the profession was not focussed upon this matter until the report of Roger and Levy Valensi[3] in 1909, who claimed that albumin was found almost constantly in the sputum in tuberculosis, but was not present in chronic bronchitis, maintaining, further, that two negative examinations of sputa for albumin excluded tuberculosis.

Naturally such statements, together with the simplicity of the test which puts it within the hands of all, at once elicited the interest of numerous observers who commenced examinations in the effort to corroborate or disprove these views. At present, however, though quite a few observers have presented the results of their studies on this subject, there is a striking lack of unanimity of interpretation of the results, particularly insofar as the test may be considered an addition to our diagnostic methods for the early recognition of tuberculosis.

The sputum for examination should be carefully collected and as little mixed with saliva as possible. Saliva contains variable amounts of protein which may react to the test for albumin, hence the sputum should be as nearly saliva-free as possible, being obtained from below the glottis. Blood in any amount and particles of food should be excluded, as they impair the accuracy of the observations. In our own tests the sputum has been collected in an open-mouthed bottle, mixed with an equal amount of tap water (though some prefer distilled water), mucin precipitated with a few drops of acetic acid, and the whole vigorously shaken and then allowed to stand. It is then filtered through a wet filter paper and the filtrate examined by any of the ordinary tests for albumin; that is, heat, 10 per cent. potassium ferrocyanide, etc.

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[2] Die Lehre vom Auswurf, Wurzburg, 1855.

[3] Société Médicale des Hôpitaux, 1909, vol. xxviii.

The question of the diagnostic and prognostic value of the reaction has divided observers into two or more classes, according to the results of their observations; opinions ranging from unqualified acceptance of the test as proof or disproof of tuberculosis to absolute disbelief in its value as a diagnostic means in tuberculosis. Brown and Ross,[4] of the Adirondack Cottage Sanitarium, conclude from an examination of the sputa of 116 cases in various stages of the disease that all patients with bacilli of tuberculosis in the sputum give a positive albumin reaction; that the degree of the reaction is proportional to the stage of the disease; that the reaction may occur only during an exacerbation of the trouble; and that a positive reaction by itself is of little diagnostic value, and in no way parallels the tuberculin tests for the determination of tuberculosis. They found that one examination was very inconclusive and on several occasions found a positive reaction after several negative findings. The repeated negative findings in cases of acute miliary tuberculosis probably mean that there is no active pulmonary tuberculosis.

Biernachi[5] says that a positive albumin reaction in the sputum has diagnostic worth only within limitations. An albumin content of more than 2 per cent. bespeaks a manifest character for the tuberculosis, a conclusion which we think will stand without fear of contradiction. An inflammatory or destructive process of lung tissue being excluded, we can, he thinks, diagnose tuberculosis upon the grounds of a positive albumin-sputum reaction.

Schmitz,[6] after an examination of the sputa of 100 cases, finds that in most cases of incipient tuberculosis, albumin is found in varying amounts in even sparse sputum without the presence of bacilli, though in undoubted cases of tuberculosis, for example, fibrosing and proliferative forms, no albumin may be found in the sputum. The albumin reaction, he concludes, is not reliable for the early diagnosis, but bears a direct relation to the degree of the illness, being greater with the progress of the disease, and hence has perhaps a value in prognosis. It bears no relation to albuminuria. However, it is so simple and easy that it is a welcome addition to our diagnostic procedures.

Eiler Hempel-Jorgensen,[7] after a series of tests (in tuberculous as well as other cases), found albumin in the sputum in ten cases of bronchitis with emphysema and asthma in varying amounts from a trace to 1.8 per cent. (3 per cent. was found in another case of bronchial asthma with bronchitis and emphysema, followed for several years without seeing any tuberculous development), and in pulmonary gangrene and croupous pneumonia. He thinks that the amount of albumin found in the sputum depends upon which part of the sputum is used and on the mechanical handling of it, since he found that there was a definite increase up to a certain moment, depending upon the amount of sputum which the patient had. He concludes, therefore, that the reaction as a diagnostic measure in the first stage of tuberculosis is not dependable.

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[4] The Albumin Reaction in the Sputum in Pulmonary Tuberculosis, Transactions of the Seventh Annual Meeting of the National Association for the Study and Prevention of Tuberculosis.

[5] Ref. by Schmey, Tuberkulose, 1911, No. 11.

[6] Die diagnostiche Bedeutung der Eiweiss-reaktion im Sputum, Med. Klinik, 20 Juli, 1913.

[7] Ueber die Eiwiss-reaktion im Sputum, Beiträge zur Klinik der Tuberkulose, vol. xxvi, No. 4.

Gelderblom,[8] in an examination of seventy-five cases, always found that a positive albumin content of the sputum meant a fresh process in the lungs, and concluded that the rise and fall of albumin in the sputum was an index to the progress of the disease. The presence of serum-albumin in the sputum seemed to confim Aufrecht's theory of the blood-borne origin of tuberculosis. He raises the interesting question, Would the systematic use of the albuminometer predict a hemorrhage?

Schneider,[9] says that Eiselt, Goodman, Fishberg and Fellerbaum, Ljubarsky, St. Acs-Nagy, and Luczinin claim that the albumin reaction in the sputum has no diagnositc significance, whereas Busnikara, Levy, Pershaw, Brunner, and Pindberg claim that it is a great aid to diagnosis. He examined the sputa of 90 cases in his series. Tuberculosis was positively diagnosed in 74 cases, 64 of which gave a positive albumin reaction in the sputum. There were 14 non-tuberculous cases, of which 8 gave a positive albumin reaction, and 2 cases, which were probably tuberculous, also had positive reactions. He divided his sputa into mucoid, mucopurulent, and purulent, and says that all pussy sputum contains albumin, the amount depending upon the pus content. He concludes that the reaction is not specific for tuberculosis, being found in 8 cases out of 14 known definitely not to be tuberculosis, and also being negative in more than 15 per cent. of cases known to be tuberculosis.

The analyses thus far reported by the writer are most discouraging, but the work of Treadgold and Ridge,[10] in a measure, contradicts the adverse reports above given. They report the results of their examinations of the sputa of 2164 cases, the largest number yet reported by any single authors. Of the first 2000 cases, 615 showed bacilli in their sputum, and in the entire series albumin was positive in 96 per cent. In the non-tuberculous cases examined albumin was found present in 32 per cent. and negative in 68 per cent. In the last 164 cases reported by them separately by reason of the greater carefulness with which the observations were made, albumin was found to be positive in 98.9 per cent. of definite tuberculosis and negative in only 1.1 per cent. Neither bacilli nor albumin were found in 25 cases of bronchitis, 2 of bronchiectasis, 1 of laryngitis, and in 14 cases clinically tuberculosis, but not active; from which observations they conclude that all active tuberculosis patients show albumin in the sputum; that the positive albumin finding in doubtful early tuberculosis supports the diagnosis; that three successive negative albumin findings with no bacilli in the sputum are strong evidence against tuberculosis; and that the test has considerable value in chronic tuberculosis and emphysema as evidence of activity when found to be positive. They have further made cytological examinations of these later specimens, and invariably found when the albumin reaction was positive there was a relative increase in the number of alveolar cells, which confirms the belief of all observers that the presence of albumin in the sputum is always associated with an alveolitis.

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[8] Deutsch. med. Woch., vol. xxxix, No. 41.

[9] Die diag. Bedeutung des Nachweiss vom Eiweiss in Sputum, Lungenkranker, Zentralblatt f. innere Med., October 1913, No. 41.

[10] The Albumin Reaction in Sputum; its Significance and Causation, Lancet, August, 1913, pp. 382 et seq.

Ritter[11] found the reaction positive in 100 per cent. of cases with bacilli and in 78 cases out of 108 suspects. Though all bacillary cases gave a positive albumin reaction the amount of the albumin was not proportionate to the number of bacilli found, just as the number of bacilli found is not always a safe index to the severity or extent of the lesion. Ritter's enthusiastic support of the test as a diagnostic measure is shown by the sub-title of his article, which reads, "Its great value as a reliable and positive diagnostic laboratory method for differentiating pulmonary tuberculosis from other pulmonary diseases."

Our cases have numbered only 20 and are too few in number from which to reach conclusions, hence this survey of the literature on the subject. They were for the most part frankly tuberculous cases and the results were not significant. We found that wherever there was an exudative process in the lungs albumin was found, the amount bearing apparently some ratio to the degree of activity though no quantitative analyses were done, and hence we cannot speak definitely on the point. In one suspicious case a sputum which showed no bacilli gave a distinct albumin reaction, the diagnosis of tuberculosis never being confirmed, though there is every indication that the patient has had a massive fibrosing pleurisy which at the present gives no evidences of activity. Just why this patient should have a positive albumin reaction in his sputum when there is no discernible evidence of alveolar trouble we are not prepared to say.

While no attempt has been made in the cases reported thus far to separate the forms of protein, it may be stated that an excess of globulin is favorable while an excess of serum-albumin is usually associated with fever, emaciation, night sweats, and an advancing process (Smolizanski). We have been able to collect from the literature the results of the analyses of 3951 cases in all stages (not including our own), in which there was a positive albumin reaction in the sputum in 3778, or 95.6 per cent. These cases were all definitely known at the time or later proved to be tuberculosis, so that the conclusion is inevitably forced upon us that the large majority of all cases of tuberculosis show a positive albumin reaction in the sputum. It is, of course, known that albumin is found in the sputum of all pneumonias, and quite frequently in caseous bronchopneumonias and cardiorenal diseases; but difficulty in differential diagnosis here from tuberculosis does not usually persist for any length of time.

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[11] The Albumin Analysis of the Sputum, Med. Rec., April 26, 1913.

From our own limited experience with the test, as well as a review of the literature on the subject, we may conclude:

1. All cases of pulmonary tuberculosis showing bacilli give a positive albumin reaction in the sputum.
2. Frequently albumin will be found in the sputum in incipient tuberculosis before bacilli are present, but its presence is variable and it cannot be relied upon as a definite means of diagnosis in incipient cases.
3. The amount of the albumin present in the sputum in tuberculosis depends upon the extent of the exudative or destructive process in the lungs, is always associated with an alveolitis, and may be an index of the activity of the process, the heavier the albumin content the more activity present.
4. Certain (fibrosing or proliferating) forms of definite tuberculosis fail to show an albumin reaction in the sputum. Cases cured for two years or more will not show it.
5. When physical signs and the tuberculin reaction fail to show activity the presence of albumin in the sputum may do so.
6. As a diagnostic means its value is limited and relative and the result of a single examination misleading. It perhaps has greater value prognostically, as above shown.
7. The test deserves wider use until its exact value has been determined.

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# A PERSONALITY STUDY OF THE EPILEPTIC CONSTITUTION.[1]

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Various mental tests in epilepsy, such as the Simon-Binet and others, have shown that there are two fairly distinguishable types

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[1] Read before the American Psychopathological Association, Albany, May 6, 1911.